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CASE REPORT

Sensitization Profiles of a Case of Pollen-Food Allergy Syndrome

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ABSTRACT

A 13-year-old girl who had had pollinosis since the age of eight began to experience itching of the ears and vomiting after eating fresh fruits such as peach, apple and watermelon. This occurred at 10 years of age. The girl displayed positive reactions to six kinds of pollens, eleven kinds of fruits, numerous vegetables and to recombinant: rBet v2 present in specific IgE antibodies. She also reacted positively to several pollens, fruits and rBet v2 in the skin prick test. In the component-resolved diagnosis (CRD) using microarray technology, she also tested positive for profilin, a pan-allergen among plants. It is reported that profilin cross-reacts between pollen, fruits, vegetables and latex. From these results, we concluded that the allergic reactions to multiple kinds of foodstuff and pollens observed in this subject were due to cross-reactivity induced by profilin. Our results demonstrate that CRD by microarray is a reliable test in the diagnosis of PFAS.

KEY WORDS

component-resolved diagnosis, IgE, microarray, pollen-food allergy syndrome, profilin, sensitization profiles

INTRODUCTION

Food allergy due to cross-reactivity between pollen allergens and fruit allergens or between pollen and vegetable allergens is termed pollen-food allergy syndrome (PFAS).[1-3] Food allergens that induce oral allergy syndrome (OAS) rapidly dissolve in the oral cavity and are readily broken down by digestive enzymes such as those present in gastric juice. These food allergens differ in properties from known food allergens, which are typically resistant to digestive enzymes and induce sensitization via the intestine. Allergies to proteins in fruits and vegetables that are cross-reactive with pollen allergens in individuals sensitized by allergens via the airway are a type of allergy termed class 2 food allergy.[4-7] This terminology distinguishes this kind of food allergy from the conventional food allergy that is caused by intestinal sensitization (class 1 food allergy).

A typical example of PFAS can be described when oral mucosal symptoms appear after a patient with a birch pollen allergy has eaten a food from the family *Rosaceous* (apple, cherry, peach, etc). Major allergens responsible for these symptoms belong to a group of allergens that exhibit high-level homology to Bet v 1, a major allergen of birch pollen, Bet v2 (profilin), and Bet v5 and 6.[1-3]

In this study, we report one case who developed immediate allergy induced by several kinds of pollens, fruits and vegetables. We performed skin prick test (SPT) and specific serum IgE antibody. In addition, we used component-resolved diagnosis (CRD) by microarray, which could screen for a large number of allergens using a small amount of serum.

CASE

A 13-year-old Japanese girl with pollinosis felt an itching sensation of her ears after eating the fruits: peach, banana, apple, melon, grapefruit, strawberry, orange, pear, and kiwi. She also felt like vomiting after having watermelon, tomato and cherry. When she wore natural rubber latex (NRL) gloves, she experienced itchiness in her hands. Other than pollinosis, she had never experienced allergic symptoms, such as atopic dermatitis or urticaria.

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Table 1 Summary of patient's examinations

		clinical symptoms	specific IgE score (FEIA) (class)	prick test (score)	scratch test (score)
fruits and vegetables	Peach	itching of ears	3	2+	3+
	Apple	itching of ears	2	2+	n.t.
	Pear	itching of ears	n.t.	2+	3+
	Strawberry	itching of ears	2	2+	3+
	Kiwi fruits	itching of ears	1	3+	n.t.
	Melon	itching of ears	3	3+	n.t.
	Orange	itching of ears	3	2+	3+
	Grapefruits	itching of ears	3	2+	2+
	Banana	itching of ears	2	1+	3+
	Cherry	vomiting	n.t.	1+	3+
	Tomato	vomiting	3	3+	n.t.
pollens	Japanese cedar		4	n.t.	n.t.
	Japanese cypress		3	n.t.	n.t.
	Japanese white birch		3	n.t.	n.t.
	Alnus		3	n.t.	n.t.
	Orchardgrass		5	4+	n.t.
	Ragweed		3	3+	n.t.
	Cross-reacting Carbohydrate Determinant (CCD)		2	n.t.	n.t.
	Latex crude allergen (clone RRIM 600)	contact urticaria	3	2+	2+
recombinant allergens	rBet v 1a		0	3+	n.t.
	rBet v 2		3	4+	n.t.
	rPru p 1		0	n.t.	n.t.
	rPru p 3		0	n.t.	n.t.
	rPru p 4		0	n.t.	n.t.
	rHevb 1		n.t.	3+	n.t.
	rHevb 5		n.t.	1+	1+
	rHevb 6.02		n.t.	1+	1+
	rHevb 8		n.t.	4+	n.t.
	rHevb 9		n.t.	1+	2+
	rHevb 10		n.t.	2+	2+
	rHevb 11		n.t.	2+	3+

Negative control (sterile physiologic saline) 0 × 0mm. n.t., not tested.
Positive control (histamine dihydrochloride; 10 mg/mL) (Wako, Japan) 3 × 3mm.

METHODS

MEASUREMENT OF SPECIFIC IMMUNOGLOBULIN (Ig) E ANTIBODIES

Commercially available assays for specific serum IgE antibodies (Immuno CAP, Phadia, Uppsala, Sweden) were performed for several pollens, vegetables, and fruits. Levels of specific IgE antibody that were >0.7 kU/L were considered positive.

SKIN PRICK TEST

We prepared the same fresh fruits and vegetables as well as extract from crude NRL (clone RRIM 600, Rubber Research Institute of Malaysia, Kuala Lumpur, Malaysia) that had caused her clinical symptoms. Recombinant (r) antigens, including rBet v 1 and 2, were purchased from BIOMAY, Vienna, Austria. Orchardgrass and ragweed were purchased from Torii Pharmaceutical, Tokyo, Japan. Prick to prick tests were performed for all fresh foods.[8] For the latex allergy, we also performed a use test.

CRD[9]

We used a commercially available allergen microar-

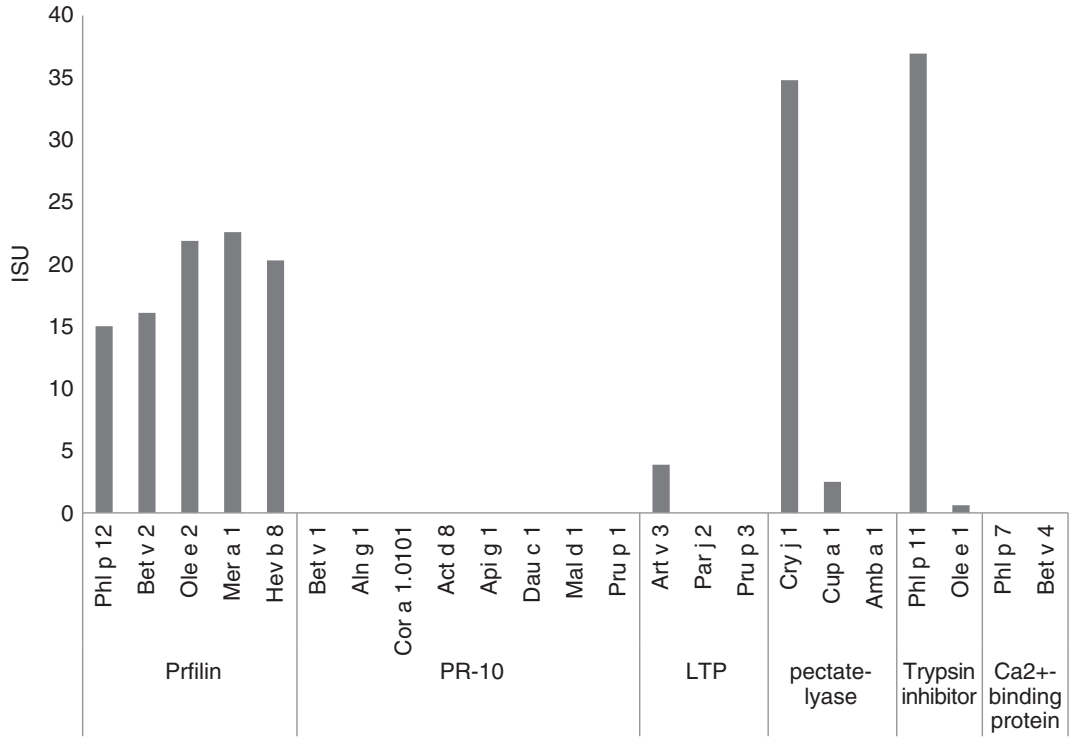

Fig. 1 The results of component-resolved diagnosis microarray; ISAC™.

ray immunoassay (immune solid phase allergen chip; ISAC™, VBC Genomics Bioscience Research, Vienna, Austria) as recommended by the manufacturer and recently described elsewhere.[10,11] Briefly, microarray reaction sites were incubated with 20 mL of undiluted patient serum for 2 h to capture allergen-specific IgE antibodies with their corresponding allergens. The microarray slides were then rinsed and washed with buffer solution in order to remove unbound serum IgE (sIgE). After drying, complexes of allergen-bound specific IgE were stained with a secondary, fluorescence-labeled anti-human IgE, for 1 h at room temperature protected from light. After a second rinsing and washing step, fluorescence signals were scanned using a laser scanner (LuxScan 10K, CapitalBio, Beijing, China). Analysis of the corresponding digitized microarray image data was performed with ImmunoCAP ISAC software. Image information was transformed into numerical data according to a reference serum with a known IgE content. Data were expressed as ISAC standardized units (ISU/L).

RESULTS

TOTAL IgE AND SPECIFIC IgE ANTIBODY (Table 1, Fig. 1)

Laboratory examinations revealed that the patient's serum total IgE titer was 620 IU/mL. Her serum tested positive for specific IgE antibodies for Japanese cedar, ragweed, white birch, Japanese cypress, Alnus, latex, peach, tomato, grapefruits, orange, melon, rBet v 2, and cross-reactive carbohydrate determinant (CCD[12]).

SPT, SCRATCH TEST AND USE TEST (Table 1, Fig. 1)

By SPT, the patient showed positive reactions to avocado, kiwi, cabbage, watermelon, tomato, melon, strawberry, orange, pear, peach, grapefruits, grape, potato, papaya, orchard grass, ragweed, rHev b8 (latex profilin) (1 μg/ml), rHev b1 (1 μg/ml), rHev b10 (1 μg/ml), rHev b11 (1 μg/ml), rBet v 2 (10 μg/ml), and Art v1a-GAM (10 μg/ml). From the scratch test, she showed positive reactions to cherry and banana. However, in the use test wearing wet a NRL glove, the result was negative.

CRD

The patient showed positive reactions to several kinds of profilin, Japanese cedar, and Phl p11,[13] yet she reacted negatively to PR-10.[14,15]

DIAGNOSIS

From these results, we were able to diagnose the patient as having PFAS. She reacted to multiple kinds of pollens (Japanese cedar, Japanese cypress, Japanese white birch, *Alnus*, orchardgrass and ragweed), and to fruits and vegetables (kiwi, banana, apple, peach, melon, grape, strawberry, orange, pear, watermelon, cherry, tomato and cabbage). She did not have latex allergy.

From sensitization profiles of ISAC, the data sug-

gested that she had been sensitized to profilin, which induced a cross-reaction to multiple pollens and foods.

DISCUSSION

OAS is an IgE-mediated immediate allergic reaction to a specific food, localized to the oral mucosa. It was first described by Amlot *et al*. in 1987,[16] yet in 1996, Lessof defined this condition as PFAS,[3] a term given to food allergies caused by a cross-reaction between pollen antigen and fruit antigens or pollen and vegetable antigens.

This patient had pollinosis since she was 8 years old. When she was 10 years of age she felt itchiness around her ears and this occurred after eating fruits. Her symptoms gradually increased with increased consumption of vegetables and fruits.

In order to identify the causative allergen of her IgE- mediated immediate allergic reaction, we performed skin prick tests and measured specific IgE levels by Immuno CAP, component resolved diagnosis microarray. These results showed she had positive reactions to several pollens, fruits and vegetables. Then, to confirm the relationships of cross-reactions amongst pollens, foods and latex, we used recombinant allergens for her test. In specific IgE assays (immunoCAP), she showed positive reactions to rHev b8 (latex profilin)[17] and rBet v2 (birch profilin), and these were the causes of her symptoms. Because she did not react in the use test with natural rubber latex, we confirmed that she did not have a latex allergy. She did however react positively to rBet v2 in the skin prick test, also in the specific IgE assays. Finally, we used the component resolved diagnosis microarray assay, a new tool for identifying specific IgE antibodies, to search through individual components of plants. We found that profilin came up with a high score in most plants. In contrast, PR-10[14,15] protein reacted negatively. Lipid transfer protein (LTP),[18] which is a causative allergen of severe allergies to vegetables and fruits, she showed a positive reaction only to Art v3 of artemisia. Specific IgE against CCD (nAna c 2), which cross-reacts to many antigens, was 1.42 IU/ml (class 2). All of these results suggested that she had class 2 allergies as she was initially sensitized to pollen and then gradually reacted to a variety of foods.

Profilin, a highly conserved 12-15 kDa protein present in all eukaryoric cells, is one of the main causes of crosssensitization between pollen and plant-derived foods.[19-22] The cross-reactivity of IgE is considered to be due to a structural similarity rather than similarity at the amino acid sequence level.[23] There major IgE epitope has been identified in birch profilin.[24] It is considered a minor pollen allergen, as it has been reported that only 10-20% of patients with pollen allergy are sensitized to this protein.[25] Asero *et al*. performed skin tests in 200 pollinosis patients using purified palm profilin (Pho d 2) and observed positive reaction in one-third of the patients.[26] The prevalence of profilin sensitization in their study was 30%, a proportion that is higher than those reported in previous studies. They considered that the difference might be due to geographical factors. There is currently no report of the profilin sensitization rate in Japan.

In this study, we report a case in which immediate allergy was induced by several kinds of pollens, fruits and vegetables. This was mediated through profilin. Although there are many unanswered questions relating to the clinical significance of profilin, we conclude that with our case, the symptoms arose from a broad cross-reactivity to profilin. Future studies will be required to elucidate further the clinical impact that profilin has in allergic reactions.

REFERENCES

1. Valenta R, Kraft D. Type 1 allergic reactions to plant-derived food: A consequence of primary sensitization to pollen allergens. *J Allergy Clin Immunol* 1996;**97**:893-5.
2. Ma S, Sicherer SH, Nowak-Wegryzyn A. A survery on the management of pollen-food allergy syndrome in allergy practices. *J Allergy Clin Immunol* 2003;**112**:784-8.
3. Lessof MH. Pollen-food allergy syndrome. *J Allergy Clin Immunol* 1996;**98**:239-40.
4. Kondo Y, Urisu A. Oral allergy syndrome. *Allergol Int* 2009;**58**:485-91.
5. Yagmi T, Haishima Y, Nakamura A, Osuna H, Ikezawa Z. Digestibility of allergens extracted from natural rubber latex and vegetable foods. *J Allergy Clin Immunol* 2000; **106**:752-62.
6. Ballmer-Weber BK, Hoffmann A, Wuthrich B *et al*. Influence of food processing on the allergenicity of celery: DBPCFC with celery spice and cooked celery in patients with celery allergy. *Allergy* 2002;**57**:228-35.
7. Bohle B, Zwolfer B, Heratizadeh A *et al*. Cooking birch pollen-related food: divergent consequences for IgE- and T cell-mediated reactivity *in vitro* and *in vivo*. *J Allergy Clin Immunol* 2006;**118**:242-9.
8. Dreborg S, Frew A. Allergen standardization and skin tests. *Allergy* 1993;**48**:49-75.
9. Ebo DG, Bridts CH, Verweij MM *et al*. Sensitization profiles in birch pollen-allergic patients with and without oral allergy syndrome to apple: lessons from multiplexed component-resolved allergy diagnosis. *Clin Exp Allergy* 2010;**40**:339-47.
10. Harwanegg C, Hiller R. Protein microarrays for the diagnosis of allergic diseases: state-of-the-art and future development. *Clin Chem Lab Med* 2005;**43**:1321-6.
11. Deinhofer K, Sevcik H, Balic N *et al*. Microarrayed allergens for IgE profiling. *Methods* 2004;**32**:249-54.
12. Aalberse RC, Koshte V, Clemens JG. Immunoglobulin E antibodies that crossreact with vegetable foods, pollen, and Hymenoptera venom. *J Allergy Clin Immunol* 1981; **68**:356-64.
13. Mari A. Skin test with a timothy grass (Phleum pretense) pollen extract vs. IgE to a timothy extract vs. IgE to rPhl p 1, rPhl p 2, nPhl p 4, rPhl p 5, rPhl p 6, rPhl p 7, rPhl p 11, and rPhl p 12: epidemiological and diagnostic data. *Clin Exp Allergy* 2003;**33**:43-51.
14. Van Loon LG, Van Strien EA. The families of

pathogenesis-related proteins, their activities, and comparative analysis of PR-1 type proteins. *Phys Mol Plant Patholl* 1999;**55**:85-97.
15. Midoro-Horiuti T, Brooks EG, Goldblum RM. Pathogenesis-related proteins of plants as allergens. *Ann Allergy Asthma Immunol* 2001;**87**:261-71.
16. Amlot PL, Kemeny DM, Zachary C, Parkes P, Lessof MH. Oral allergy syndrome (OAS): symptoms of IgE-mediated hypersensitivity to foods. *Clin Allergy* 1987;**17**:33-42.
17. Diez-Fomez ML, Quirce S, Cuevas M *et al*. Fruit-pollen-latex cross-reactivity: implication of profilin (Bet v2). *Allergy* 1999;**54**:951-61.
18. Garcia Ortiz JC, Cosmes PM, Lopez-Asunsolo A. Allergy to foods in patients monosensitized to Artemisia pollen. *Allergy* 1996;**51**:927-31.
19. Valenta R, Duchene M, Ebner C *et al*. Profilins constitute a novel family of functional plant pan-allergens. *J Exp Med* 1992;**175**:377-85.
20. Ebner C, Hirschwehr R, Bauer L *et al*. Identification of allergens in fruits and vegetables: IgE cross-reactivities with the important birch pollen allergens Bet v 1 and Bet v 2 (birch profilin). *J Allergy Clin Immunol* 1995;**95**:962-9.
21. Valenta R, Duchene M, Pettenburger K *et al*. Identification of profilin as a novel pollen allergen; IgE autoreactivity in sensitized individuals. *Science* 1991;**253**:557-60.
22. Van Ree R, Voitenko V, van Leeuwen WA, Aalberse RC. Profilin is a cross-reacting allergen in pollen and vegetable food. *Int Arch Allergy Immunol* 1992;**98**:97-104.
23. Rihs HP, Chen Z, Rueff F *et al*. IgE binding of the recombinant allergen soybean profilin (rGly m 3) is mediated by conformational epitopes. *J Allergy Clin Immunol* 1999; **104**:1293-301.
24. Fedorov AA, Ball T, Mahoney NM, Valenta R, Almo SC. The molecular basis for allergen cross-reactivity: crystal structure and IgE-epitope mapping of birch pollen profilin. *Structure* 1997;**5**:33-45.
25. Pauli G, Oster JP, Deviller P *et al*. Skin testing with recombinant allergens rBet v 1 and birch profilin, rBet v 2: diagnostic value for birch pollen and associated allergies. *J Allergy Clin Immunol* 1996;**97**:1100-9.
26. Asero R, Monsalve R, Barber D. Profilin sensitization detected in the office by skin prick test: a study of prevalence and clinical relevance of profilin as a plant food allergen. *Clin Exp Allergy* 2008;**38**:1033-7.